REMARKS

Applicant timely submits this response to the Examiner's Office Action of January 24, 2005, the period for response to which has been extended three months to July 25, 2005.

Claims 1, 20, 11, 12, and 24 have been amended and claims 3 and 26-41 have been cancelled. Claims 42–57 are newly added. Upon entry of the foregoing amendment, claims 1, 5-8, 10-12, 17-19, 21-25 and 42-57 will be pending.

Applicants respectfully submit that no prohibited new matter has been introduced by the amendments. Written description support for the new claims can be found throughout the specification. For example, support for the amendments to claim 1 can be found throughout the specification, but specifically on pages 3, 4, 8 and 20. Support for the amendments to claim 10 can be found throughout the specification, but specifically on page 15. Support for the amendments to claim 11 can be found throughout the specification and specifically on pages 11 and 12 and original claim 11. Support for the amendments to claim 12 are found on page 12. Support for the amendment to claim 24 can be found throughout the specification and specifically on pages 3, 4, 7 and 8. Support for new claims 42 and 43 may be found on pages 9, 15 and 20. Support for new claims 46-48 may be found on pages 4, 6 and 7. Support for new claim 49 may be found on page 12. Support for new claim 50 may be found on page 16. Support for new claims 52 and 53 may be found in original claim 2 and on pages 3 and 4. Support for new claims 54-57 may be found on page 20.

The Office Action has been carefully reviewed and the following remarks are made in response thereto. In view of the amendments and following remarks, Applicant respectfully requests reconsideration and reexamination of this application and the timely allowance of the pending claims.

I. Summary of the Office Action

1. Upon entry of the attached amendment, claims 1, 5-8, 10-12, 17-19, 21-25, and 42-57 will be pending.

2. Claims 17-19, 21-29, 33, 37, and 41 are rejected under 35 U.S.C. § 112, first paragraph, for purportedly insufficient written description for methods of treating "neurogenic inflammation."

3. Claims 1, 3, 5-8, 10-12, 17-19, and 21-41 are rejected under 35 U.S.C. § 112, first paragraph, for purportedly insufficient written description for: i) a first patient identification step (claims 1, 10, 11, and 24); ii) a method comprising blocking nerve and mast cell release of preformed mediators that produce permeability (claims 19 and 26); iii) a method comprising administering botulinum toxin in a dose that is lower than that necessary to produce regional muscle weakness (claims 30-33); and iv) a method wherein the botulinum toxin dose is between 2 and 60 units (claims 34-37).

4. Claims 3 and 30-33 are rejected under 35 U.S.C. § 112, first paragraph, for purportedly lacking an enabling disclosure for methods of treating inflammation that do not produce "substantial muscle weakness."

5. Claims 1, 5, 6, 17-29, 34, 37, 38 and 41 were rejected under 35 U.S.C. §102(e) as purportedly anticipated by First. (U.S. Patent 6,063,768).

6. Claims 1, 5, 34, and 38 were rejected under 35 U.S.C. §102(b) as purportedly anticipated by Pasricha *et al.* (U.S. Patent No. 5,437,291).

7. Claims 1, 5-8, 10-12, 17-29, and 34-41 were rejected under 35 U.S.C. §103(a) as purportedly obvious over First in view of the Merck Manual.

8. No claims were allowed.

II. Response to the Office Action

1. Rejection of the claims under 35 U.S.C. § 112, first paragraph, as purportedly not enabled.

Claims 3 and 30-33 were rejected under 35 U.S.C. § 112, first paragraph, for purportedly not enabling the claimed invention for claims drawn to methods of reducing inflammation without causing substantial muscle weakness. Applicant respectfully traverses this rejection.

Claims 3 and 30-33 have been cancelled. Claims 1, 5-8, 24 and 25 have been amended to recite a dose "sufficient to reduce the at least one symptom of inflammation but less than a dose necessary to produce substantial muscle weakness within said affected area." New claims 42, 43 and 46-57 also include a dose that does not produce substantial muscle weakness in the affected area of a treated subject.

The Examiner alleges that claims drawn to methods of reducing inflammation without producing substantial muscle weakness are not enabled, because this response is "inherently unpredictable" and requires "some sort of enablement in addition to mere assertion." (See page 4 of Office Action). Applicants respectfully submit that the instant specification fully enables the skilled artisan to make and use the claimed invention. Specifically, the instant disclosure teaches in the first lines of the "Summary of Invention" (pages 3 and 4) that "the use of botulinum toxin in doses from 1/3rd to several orders of magnitude less than those associated with treatment of regional movement diseases has been effective to reduce inflammation and adverse sensory experiences associated with the inflammatory response." Further, "[T]ypical minimum effective dosages range form 0.5-5 units as opposed to 20-600 units for the treatment of movement disorders." The lower dose range is effective in reducing inflammation and is below the dose necessary to treat movement disorders—a treatment that necessarily produces muscle weakness.

Variations in the doses necessary for the treatment of movement disorders reflect the variation in the size and volume of a treated muscle, as well as the severity of the treated condition. Accordingly, the appropriate dose sufficient to treat a movement disorder will vary depending upon the affected muscle or area. Because the instant

specification—throughout the disclosure—teaches dosing levels that reduce inflammation without producing sufficient muscle weakness and specifically doses from 1/3rd to several orders of magnitude less than those associated with treatment of regional movement disorders in the corresponding muscle, the instant specification enables a skilled artisan to practice that claimed invention without undue experimentation.

In view of the foregoing amendments and remarks, Applicant respectfully requests withdrawal of the outstanding enablement rejection to the extent it may be applied to new claims 42, 43 and 46-57.

2. Rejection of the claims under 35 U.S.C. § 112, first paragraph, as purportedly lacking written description.

Claims 17-19, 21-29, 33 and 37 were rejected under 35 U.S.C. § 112, first paragraph, for purportedly not providing an adequate written description of the claimed invention. The Examiner concludes "that the specification cannot support claims amended to recite a method for treating neurogenic inflammation." (Final Office Action of September 25, 2003, page 5).

Claims 17-19 and 21-23 were timely copied from U.S. Patent No. 6,063,768 (the '768 patent) to First and are subject a request that an interference be declared between the '768 patent and the pending claims.

Amended claims 24 and 25 (dependent on claim 24) are drawn methods of treating inflammation and do not recite the phrase "neurogenic inflammation." Claims 26-29, 33 and 37 have been cancelled. Accordingly, Applicants respectfully request withdrawal of this rejection as applied to the claims 24 and 25 and a grant of benefit of priority to U.S. Provisional Application Serial No. 60/097,846.

Claims 1, 3, 5-8, 10-12, 17-19, and 21-41 are rejected under 35 U.S.C. § 112, first paragraph, for purportedly insufficient written description for: i) a first patient identification step (claims 1, 10, 11, and 24); ii) a method comprising blocking nerve and mast cell release of preformed mediators that produce permeability (claims 19 and 26); iii) a method comprising administering botulinum toxin in a dose that is lower than that

necessary to produce regional muscle weakness (claims 30-33); and iv) a method wherein the botulinum toxin dose is between 2 and 60 units (claims 34-37).

Claims 3 and 26-41 have been cancelled. Claims 1, 10, 11 and 24 have been amended to remove the first patient selection step and express written description support for "blocking nerve and mast cell release of preformed mediators that produce vasodilation and permeability, altered sensory experience, edema and/or erythema" (claim 19) can be found on page 4, lines 16-18 of the instant specification. Accordingly, in view of the foregoing amendments and remarks, Applicant respectfully requests that the Examiner grant benefit of priority to U.S. Provisional Application Serial No. 60/097,846 and withdraw the outstanding written description rejection of claims 1, 10, 11, 19 and 24.

3. Rejection of the claims under 35 U.S.C. § 102(e) as purportedly anticipated by First.

Claims 1, 5, 6, 17-19 and 21-29, 34, 37, 38 and 41 were rejected under 35 U.S.C. §102(e) as purportedly anticipated by First. (U.S. Patent 6,063,768).

Claims 26-41 have been cancelled. As the Examiner has acknowledged by not applying the '768 patent to claims 3, 10, 11, 12 and 30-33, the '768 patent to First does not teach methods of treating allergic blepharoconjunctivitis (claim 10), classic type 1 hypersensitivity (claim 11) or inflammation with a dose sufficient to reduce at least one symptom of inflammation but less than a dose necessary to produce substantial muscle weakness within said affected area (claims 3 and 30-33). Accordingly, Applicants respectfully request withdrawal of this rejection as it is applied to claims 1, 5, 6, 24 and 25 and as it may be applied to new claims 42-57.

Applicant notes that a Request to Declare an Interference between claims 17-19 and 21-23 of the instant application and the First patent was submitted on May 14, 2001. Once these claims are determined to be otherwise allowable, the Examiner may determine if an interference should be declared.

4. Rejection of the claims under 35 U.S.C. § 102(b) as purportedly anticipated by Pasricha *et al.*

Claims 1, 5, 34, and 38 were rejected under 35 U.S.C. §102(b) as purportedly anticipated by Pasricha *et al.* (U.S. Patent No. 5,437,291).

Claims 34 and 38 have been cancelled. Claims 1 and 5 (claim 5 depends from claim 1) are drawn to methods of treating inflammation with a dose sufficient to reduce at least one symptom of inflammation but less than a dose necessary to produce substantial muscle weakness within said affected area. As the Examiner has acknowledged by not applying the '291 patent to claims 3 and 30-33, the '291 patent to Pasricha *et al.* does not teach methods of treating inflammation with a dose sufficient to reduce at least one symptom of inflammation but less than a dose necessary to produce substantial muscle weakness within said affected area. Accordingly, Applicants respectfully request withdrawal of this rejection as it is applied to claims 1 and 5 and as it may be applied to new claims 42-57.

5. Rejection of the claims under 35 U.S.C. § 103(a) as purportedly obvious over First in view of the Merck Manual.

Claims 1, 5-8, 10-12, 17-29, and 34-41 were rejected under 35 U.S.C. §103(a) as purportedly obvious over First in view of the Merck Manual.

Claims 20 and 26-41 are cancelled. As the Examiner has acknowledged by not applying the '768 patent to claims 3, 10, 11, 12 and 30-33, the '768 patent to First does not teach methods of treating allergic blepharoconjunctivitis (claim 10), classic type 1 hypersensitivity (claim 11) or inflammation with a dose sufficient to reduce at least one symptom of inflammation but less than a dose necessary to produce substantial muscle weakness within said affected area (claims 3 and 30-33). Accordingly, Applicants respectfully request withdrawal of this rejection as it is applied to claims 1, 5-8, 10-12, 24, and 25 and as it may be applied to new claims 42-57.

Applicant notes that a Request to Declare an Interference between claims 17-19 and 21-23 of the instant application and the First patent was submitted on May 14, 2001.

Once these claims are determined to be otherwise allowable, the Examiner may determine if an interference should be declared.

III. CONCLUSION

Applicant believes that the above-referenced application is in condition for allowance. Reconsideration and withdrawal of the outstanding rejections and early notice of allowable subject matter to that effect is respectfully requested.

EXCEPT for issue fees payable under 37 C.F.R. § 1.18, the Director is hereby authorized by this paper to charge any additional fees during the entire pendency of this application, including fees due under 37 C.F.R. §§ 1.16 and 1.17 which may be required, including any required extension of time fees, or credit any overpayment to Deposit Account No. 13-3250, reference No. 33677.00600. This paragraph is intended to be a **CONSTRUCTIVE PETITION FOR EXTENSION OF TIME** in accordance with 37 C.F. R. § 1.136(a)(3).

If the Examiner finds that a telephone conference would further prosecution of this application, the Examiner is invited to contact the undersigned at 202-835-7553.

Respectfully submitted,

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